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?show files;ds
File 350:Derwent WPIX 1963-2002/UD,UM &UP=200256
         (c) 2002  Thomson Derwent
File 344:Chinese Patents Abs Aug 1985-2002/Aug
         (c) 2002 European Patent Office
File 347:JAPIO Oct 1976-2002/Apr(Updated 020805)
         (c) 2002 JPO & JAPIO
File 371:French Patents 1961-2002/BOPI 200209
         (c) 2002 INPI.  All rts. reserv.

Set     Items   Description
S1     228454   PROFILE OR PROFILES OR PROFILING OR SET(2W)(DATA OR CHARAC-
              TERISTIC? ? OR FEATURE? ?) OR TRAIT? ? OR REPRESENTATION
S2     122163   (MEDICAL OR HEALTH OR BIOLOGICAL)(2W)(CONDITION? ? OR DISE-
              ASE? ? OR STATUS) OR DISEASE? ? OR ILLNESS OR ILLNESSES
S3     376219   BODY()PART? ? OR PART? ?(4N)BODY OR ORGAN? ? OR BIOLOGICAL-
              ()SYSTEM? ? OR (NERVOUS OR SKELETAL OR HUMAN()BODY OR IMMUNE -
              OR CARDIOVASCULAR OR RESPIRATORY OR MUSCULAR OR LYMPHATIC OR -
              DIGESTIVE)(2W)SYSTEM? ? OR KIDNEY? ? OR HEART OR BRAIN
S4      25222   LUNG? ? OR BLOOD()PRESSURE
S5    3892628   CAPACITY OR THROUGHPUT OR THROUGH()PUT OR VOLUME OR POWER -
              OR EFFICACY OR CONDITION OR LEVEL OR CAPABILITY OR ABILITY OR
              FUNCTION?
S6       4390   S4(6N)(ASSESS? OR ESTIMAT? OR ANALYS? OR ANALYZ? OR DETERM-
              IN? OR PREDICT? OR MEASUR? OR CALCULAT? OR COMPUTE OR COMPUTI-
              NG OR COMPUTES OR EVALUAT? OR TEST?)
S7    2955920   TIME OR DISTRIBUTION OR AVERAGE OR AVERAGING OR OVERTIME OR
               DELTA
S8       6379   S2(6N)(ASSESS? OR ESTIMAT? OR ANALYS? OR ANALYZ? OR DETERM-
              IN? OR PREDICT? OR MEASUR? OR CALCULAT? OR COMPUTE OR COMPUTI-
              NG OR COMPUTES OR EVALUAT? OR TEST?)
S9     242184   S5(6N)(ASSESS? OR ESTIMAT? OR ANALYS? OR ANALYZ? OR DETERM-
              IN? OR PREDICT? OR MEASUR? OR CALCULAT? OR COMPUTE OR COMPUTI-
              NG OR COMPUTES OR EVALUAT? OR TEST?)
S10      1386   S8 AND S9
S11       218   S1 AND S10
S12        38   S7 AND S11
S13         7   S12 AND IC=G06F
S14        31   S12 NOT S13
?
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?t13/4/all

13/4/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

IM- *Image available*
AA- 2002-351288/200238|
XR- <XRAM> C02-099689|
XR- <XRPX> N02-276066|
TI- Estimating haplotype frequencies to detect linkage between particular haplotype and **disease** state, by **estimating** haplotype frequencies from unphased diploid genotype data using Estimation-Maximization algorithm|
PA- GENSET (GEST); FALLIN D (FALL-I); LISSARRAGUE S (LISS-I); SCHORK N J (SCHO-I)|
AU- <INVENTORS> FALLIN D; LISSARRAGUE S; SCHORK N J; SCHORK N|
NC- 094|
NP- 003|
PN- WO 200191026 A2 20011129 WO 2001IB1284 A 20010522 200238 B|
PN- AU 200169382 A 20011203 AU 200169382 A 20010522 200238
PN- US 20020077775 A1 20020620 US 2000207904 P 20000525 200244
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<AN> US 2000635502 A 20000809
<AN> US 2001818260 A 20010326|
AN- <LOCAL> WO 2001IB1284 A 20010522; AU 200169382 A 20010522; US 2000207904 P 20000525; US 2000221850 P 20000728; US 2000635502 A 20000809; US 2001818260 A 20010326|
AN- <PR> US 2001818260 A 20010326; US 2000207904 P 20000525; US 2000221850 P 20000728; US 2000635502 A 20000809|
FD- WO 200191026 A2 G06F-019/00
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<DS> (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
FD- AU 200169382 A G06F-019/00 Based on patent WO 200191026
FD- US 20020077775 A1 G06F-017/18 Provisional application US 2000207904
Provisional application US 2000221850
Cont of application US 2000635502|
LA- WO 200191026(E<PG> 69)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW|
DS- <REGIONAL> AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; MZ; NL; OA; PT; SD; SE; SL; SZ; TR; TZ; UG; ZW|
AB- <PN> WO 200191026 A2|
AB- <NV> NOVELTY - Estimating (M1) haplotype frequencies for single nucleotide polymorphisms (SNP) in groups of individuals, comprises estimating all haplotype and diplotype probabilities for the groups of individuals using an Estimation-Maximization (E-M) process, storing the probabilities and repeating the E-M process using random starting values.|
AB- <BASIC> DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a method (M2) of determining the statistical significance of a difference between haplotype frequency **profiles** of at least two groups of individuals;
(2) a system comprising instructions or modules configured for performing M2;

(3) a computer system for estimating haplotype frequencies for SNP in groups of individuals and for detecting association between a haplotype and phenotype;

(4) wide area computer network for executing M2, comprising:

(a) a server comprising SNP; and

(b) a workstation comprising instructions for estimating haplotype frequencies using the nucleotide polymorphism data for each group individually and in combination with the other group, where all haplotype and diplotype probabilities are calculated once and are stored, and where the maximization process is automatically repeated using random starting values.

(5) a method (M3) for determining an association between a haplotype and a phenotype;

(6) a method (M4) for detecting an association between a haplotype and a phenotype;

(7) a system comprising instructions for performing M2 or M4;

(8) a programmed storage device for performing M1, M2, M3 or M4;

(9) a computer-readable data signal embedded in a transmission medium that when executed, performs M2 or M4; and

(10) a computer system, preferably a wide area computer system, for performing M3.

USE - For estimating haplotype frequencies for SNPs in groups of individuals, which is useful for determining linkage between a haplotype and a phenotype (claimed).

ADVANTAGE - Unlike many haplotype analysis methods that require phase information that can be difficult to obtain from samples of non-haploid species, the method based on E-M algorithm overcomes the missing phase information.

DESCRIPTION OF DRAWING(S) - The figure shows the block diagram beginning with haplotype estimation, continuing through use of a test statistic and ending after an interference drawing procedure.

pp; 69 DwgNo 1/16|

AB- <TF> TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: In M1, all the haplotypes are coded with binary mask arrays, and identical genotypes are grouped prior to performing the estimations.

M2 comprises:

(a) determining the combined likelihood that at least 2 groups of individuals are derived from the same **distribution** of haplotypes;

(b) determining the sum of the separate likelihoods that each of the two groups of individuals are derived from the same **distribution** of haplotypes;

(c) determining the difference of the sum and the combined likelihood; and

(d) determining the significance of this difference by stimulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same **distribution** of haplotypes.

The method further comprises calculating all possible single-haplotype chi-square tests prior to determining the significance of the difference between the sum and the combined likelihood. The method further comprises assessing the statistical significance of individual haplotypes using an odds ration or à P-excess value.

Alternatively, M2 comprises:

(a) estimating haplotype frequencies using single nucleotide polymorphism data for each group individually and for each group in combination with another group, where all haplotype and diplotype probabilities are calculated once and then stored, where a maximization process is automatically repeated for each group using random starting values in order to determine final likelihoods;

(b) comparing the final likelihood that all groups come from the same **distribution** of haplotypes with the sum of the final likelihoods for each group separately to determine their difference; and

(c) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same **distribution** of haplotypes.

All the haplotypes are coded with binary mask arrays, and identical genotypes are grouped prior to performing the estimationsM3 comprises:

(a) estimating haplotype frequencies using single nucleotide polymorphism data for an affected group and an unaffected group individually and in combination with another group, where all haplotype and diplotype probabilities are calculated once and then stored, where a maximization process is automatically repeated for each group using random starting values in order to determine final likelihoods;

(b) comparing the final likelihood that all groups come from the same **distribution** of haplotypes with the sum of the final likelihoods for each group separately to determine their difference; and

(c) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same **distribution** of haplotypes and determine whether a statistically significant association exists between the haplotype and the phenotype.

Alternatively, M3 comprises:

(a) estimating haplotype frequencies using single nucleotide polymorphism data for an affected group and an unaffected group individually and in combination with another group, where all haplotype and diplotype probabilities are calculated once and then stored; and

(b) repeating a maximization process for each group using random starting values to determine whether a statistically significant association exists between the haplotype and phenotype.

M4 comprises:

(a) comparing the final likelihood that members of an affected group and an unaffected group come from the same **distribution** of haplotypes with the sum of the final likelihoods for each group separately to determine their difference; and

(b) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same **distribution** of haplotypes and whether a statistically significant association exists between the haplotype and phenotype.

COMPUTING AND CONTROL - Preferred Computer System: All the haplotypes are coded with binary mask arrays, and identical genotypes are grouped prior to performing the estimations.

Preferred Computer Network: The network comprises the internet. The instructions are stored in memory or in a code segment.

Preferred Storage Device: The programmed storage device of (9) comprisesa) determining the statistical significance of the difference between haplotype frequency **profiles** of at least 2 groups of individuals by comparing the final likelihood that all groups of individuals come from the same **distribution** of haplotypes with the sum of the final likelihoods for each group separately; and

(b) determining the significance of this difference by stimulating hypothetical groups by randomly permuting between groups to determine the probability that the groups do not come from the same **distribution** of haplotypes.

The storage device further comprises instructions that when executed perform a method of calculating all possible single-haplotype chi-square tests prior to determine the significance of the difference between the sum and the combined likelihood. The device further comprises instruction that when executed perform a methods of assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value.

Alternatively, the storage device comprising E-M instructions that when executed performs M1|

AB- <XA> EXAMPLE - To test the accuracy of haplotype estimation using the methods described above, the error between Estimation-Maximization (E-M)-based haplotype frequency estimates and either haplotype frequencies observed in particular data sets or the true haplotype frequencies in the population at large, was **assessed** as a **function** of several population and data **set characteristics** . The possible factors influencing the accuracy of the method include sample size (and sampling error), proportion of ambiguous individuals/heterozygous loci, presence of Hardy-Weinberg equilibrium (HWE), haplotype and allele frequencies, number of loci in haplotype, and level of linkage disequilibrium in the area. Sample diploid data sets were simulated using computer programs that perform one embodiment of our method under different generating (or true population) scenarios. The 'accuracy' of the method was assessed by comparing the final estimated haplotype frequencies (Ef) to either the original generating frequencies (population parameters (Gf)), or to the haplotype frequencies in a sample drawn from the simulation parameters (which are different than the generating frequencies due to sampling error/chance (Sf)). If the main interest was assessing the overall validity of haplotype estimates representative of the true population parameters, the comparison of interest would be the estimated versus generating values. However, this comparison includes the effect of sampling error, which would exist for the phase-known methods. A more relevant comparison for practical purposes, then, would be the accuracy of a haplotype estimation from a sample diploid set (simulated from the generating parameters), as this more closely reflects any additional error incurred by our estimation procedures relative to phase-known methods from population samples. Simulation Data sets of varying sample sizes were simulated by randomly assigning haplotypes with a specific number of di-allelic loci to all individuals. Haplotype frequencies were either constrained to be equally frequent (each=1/2L) among the n individuals, or were generated according to a specified variance parameter indicating amount of departure from uniformly distributed frequencies. For example, a simulation with haplotype frequency variance set at 10, would generate and randomly assign haplotypes among the n individuals according to a **distribution** with mean 1/2L and variance 10, resulting in very large discrepancies between haplotype frequencies within the data set. Simulation in this way is not based on a particular population genetics model, but samples over many underlying allele and haplotype frequencies, allelic association strengths, and Hardy-Weinberg scenarios, allowing for the assessment of the influence of such characteristics on estimation validity. The choice of accuracy measurement depends on the study goals. The most interesting result is the accurate estimation of haplotype frequencies, rather than the identification of any particular haplotype. Thus, we have used two measures of accuracy for frequency comparison - absolute difference (or bias) between the estimated frequency of any randomly chosen haplotype and its frequency in the comparison sample or population, and the mean squared error between all haplotypes of the two comparison groups. In a 2-locus system, the absolute difference between the generating, sample, and estimated haplotype frequencies, could be calculated for all four possible haplotypes. For example, the bias between the frequency of haplotype 1, h1, from the generating parameters and the final estimated frequency would be G1 - E1. However, as the number of loci increase, recording this value for every possible haplotype and every possible comparison would be prohibitive. Instead, the absolute bias was calculated for the most and least frequent haplotypes, as well as for a random estimated haplotype from each simulated data set. In order to incorporate differences among all haplotypes, and to standardize for the number of possible haplotypes in a data set, the mean standard error between the three stages (generating, simulated sample, and estimated haplotypes) was also calculated. For example, the mean

standard error (MSE) of estimates compared to generating values would be MSEg-e=SIGMAh(Eh-Gh)2/Nh for h=1..2L.

To set optimal conditions for measuring the effect of population and data **set characteristics** on the haplotype estimation accuracy, the influence of several program specifications were assessed, including restarts, number of iterations, and the size of the convergence criterion. It was found that because the E-M algorithm may converge slowly and to a local maximum, the program should be restarted several times, with different initial values, ample iterations, and a small enough convergence criterion to achieve the global maximum. Varying these three programming options can guide the most efficient maximization. The **distribution** of resulting log-likelihoods and error measurements also provides an indication of the correctness of the maximization process. The result shows the expected increase and plateau of log-likelihoods as the three options become increasingly liberal for runs performed on the same batch of 500 simulated data sets. From these results, setting the program for 10 restarts, setting maxit=150, and convergence to 0.00001, should be reasonably efficient. These settings were then used for all subsequent program runs described in the following sections. There was no apparent trend in mean squared error or bias between the **estimates** and sample/generating values as a **function** of these settings, although the standard deviation of the averaged maximum log-likelihoods decreases as the settings become more liberal. In this situation, each batch is a new **set** of simulated **data** sets, as opposed to the results shown in the specification in which all runs were performed on the same batch of 500 simulated sets such that likelihoods were comparable.|

DE- <TITLE TERMS> ESTIMATE; FREQUENCY; DETECT; LINK; DISEASE; STATE; ESTIMATE; FREQUENCY; DIPLOID; GENOTYPE; DATA; ESTIMATE; MAXIMISE; ALGORITHM|
DC- B04; D16; T01|
IC- <MAIN> **G06F-017/18 ; G06F-019/00** |
MC- <CPI> B04-E03; B11-C08F1; B12-K04F; D05-H09|
MC- <EPI> T01-J|
FS- CPI; EPI||

13/4/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

IM- *Image available*
AA- 2002-257113/200230|
XR- <XRPX> N02-199076|
TI- Computational system e.g. for modelling protein expression in an organ, where the organ model can be used to explore and model the impact of genetic and sex linked cellular changes on the organ|
PA- PHYSIOME SCI INC (PHYS-N)|
AU- <INVENTORS> COLATSKY T J; MUZIKANT A L; RICE J J; ROUNDS D|
NC- 094|
NP- 002|
PN- WO 200198935 A2 20011227 WO 2001US19918 A 20010622 200230 B|
PN- AU 200168668 A 20020102 AU 200168668 A 20010622 200230|
AN- <LOCAL> WO 2001US19918 A 20010622; AU 200168668 A 20010622|
AN- <PR> US 2000599128 A 20000622|
FD- WO 200198935 A2 G06F-017/00
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FD- AU 200168668 A G06F-017/00 Based on patent WO 200198935|
LA- WO 200198935(E<PG> 26)|
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DS- <REGIONAL> AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; MZ; NL; OA; PT; SD; SE; SL; SZ; TR; TZ; UG; ZW|
AB- <PN> WO 200198935 A2|
AB- <NV> NOVELTY - Computational model of an organ which allows a process for assessing the microscopic and whole organ impact of genetic differences that occur in single cells comprising the organ. The genetic differences in the model are based on changes on protein function or **distribution** associated with genetic mutations, gender, disease or allele based variations in the pattern of gene expression.|
AB- <BASIC> DETAILED DESCRIPTION - INDEPENDENT CLAIM is also included for the following: computational model of a heart

USE - For modelling protein expression in an organ.

ADVANTAGE - This technique is useful for determining the impact of a mutation or sex on the performance of an otherwise equivalent organ. The ability to model some sex based changes and to ignore others within the model domain is a very useful and a feature not easily available in physical models. The utility of this modelling process is the **ability** to **determine** mutation induced changes in response to **disease** , drugs, or other perturbations in transmembrane potential. The organ model is also useful for determining differences in the response to drugs, genetic mutations, or disease expression related to sex and allelic variations in cellular background.

DESCRIPTION OF DRAWING(S) - The diagram shows a simplified flow chart describing the creation and computation of the model, and an alternate schematic **representation** of the model and the model building process

data (10)
AP (16,18)
ECG (30,24,26,28)
pp; 26 DwgNo 1/7|

DE- <TITLE TERMS> COMPUTATION; SYSTEM; MODEL; PROTEIN; EXPRESS; ORGAN; ORGAN; MODEL; CAN; MODEL; IMPACT; GENETIC; SEX; LINK; CELLULAR; CHANGE; ORGAN|
DC- S05; T01|
IC- <MAIN> **G06F-017/00** |
MC- <EPI> S05-P; T01-J06A; T01-J15H|
FS- EPI||

13/4/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

AA- 2002-195970/200225|
XR- <XRAM> C02-060641|
TI- Identifying paramyxovirus heamagglutinin neuraminidase (HN) inhibitor useful for treating or preventing croup, by applying three-dimensional structure of active site of paramyxovirus HN to design or select inhibitor|
PA- BIOCRYST PHARM INC (BIOC-N); ST JUDE CHILDREN'S RES HOSPITAL (SJUD-N); UNIV BATH (UYBA-N); UNIV ST ANDREWS (UYSA-N); BABU Y S (BABU-I); PORTNER A (PORT-I); ROWLAND R S (ROWL-I); TAKIMOTO T (TAKI-I); TAYLOR G (TAYL-I)|
AU- <INVENTORS> BABU Y S; PORTNER A; ROWLAND R S; TAKIMOTO T; TAYLOR G; TAKOMOTO T|
NC- 094|

NP- 003|
PN- WO 200210459 A2 20020207 WO 2001US23623 A 20010727 200225 B|
PN- AU 200183000 A 20020213 AU 200183000 A 20010727 200238
PN- US 20020081572 A1 20020627 US 2000221199 P 20000727 200245
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AN- <LOCAL> WO 2001US23623 A 20010727; AU 200183000 A 20010727; US 2000221199 P 20000727; US 2001915515 A 20010727|
AN- <PR> US 2000221199 P 20000727; US 2001915515 A 20010727|
FD- WO 200210459 A2 C12Q-001/70
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FD- AU 200183000 A C12Q-001/70 Based on patent WO 200210459
FD- US 20020081572 A1 C12Q-001/70 Provisional application US 2000221199|
LA- WO 200210459(E<PG> 30)|
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DS- <REGIONAL> AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; MZ; NL; OA; PT; SD; SE; SL; SZ; TR; TZ; UG; ZW|
AB- <PN> WO 200210459 A2|
AB- <NV> NOVELTY - Identifying (M1) a potential inhibitor (I) for a paramyxovirus Hemagglutinin-neuraminidase (HN) involves using a three-dimensional (3D) structure of (active site groups of) paramyxovirus HN, applying the 3D structure to design or select (I), and associating (I) obtained with the enzyme in presence of substrate to **determine** the **ability** of (I) to inhibit the enzyme.|
AB- <BASIC> DETAILED DESCRIPTION - Identifying a potential inhibitor (I) for a paramyxovirus Hemagglutinin-neuraminidase (HN) involves using a three-dimensional (3D) structure of paramyxovirus HN as defined by the structure coordinates comprising the amino acid residues (R) 174, 175, 190, 192, 199, 234, 236, 237, 254, 256, 258, 262, 299, 302, 317, 363, 364, 369, 401, 416, 466, 498 or 526 of a fully defined sequence of 577 amino acids (S1) as given in the specification, applying the 3D structure to design or select (I), and associating (I) obtained with the enzyme in presence of substrate to **determine** the **ability** of (I) to inhibit the enzyme.

INDEPENDENT CLAIMS are also included for the following:

(1) a complex (II) of a paramyxovirus HN and a substrate or inhibitor molecule;

(2) a machine-readable data storage medium (III) comprising a data storage material encoded with machine-readable data which comprises structure coordinates comprising (R) of (S1); and

(3) a computer (IV) for producing a 3D **representation** of a molecule or molecular complex, where the molecule or molecular complex comprises a binding pocket defined by structure coordinates comprising (R) of (S1), where the computer comprises (III), working memory for storing instructions for processing the machine-readable data; a central processing unit coupled to the working memory and to (III) for processing the machine readable data into the 3D **representation** ; and a display coupled to the central-processing unit for displaying the 3D **representation** .

ACTIVITY - Antiinflammatory; virucide.

No supporting biological data is given.

MECHANISM OF ACTION - Paramyxovirus heamagglutinin-neuraminidase inhibitor.

No supporting biological data is given.

USE - For identifying a potential inhibitor of paramyxovirus HN

(claimed). (I) identified by (M1) is useful for treating or preventing undesired properties of infection by paramyxoviruses, and thus for treating or preventing croup, bronchitis, pneumonia, or any other respiratory disease caused by paramyxovirus.

pp; 30 DwgNo 0/5|

AB- <TF> TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: (I), a competitive, non-competitive, or uncompetitive inhibitor of a paramyxovirus HN, is designed de novo or from a known inhibitor. (I) is designed to form salt links with Arg416 and Arg498 of a paramyxovirus HN, hydrogen bonds or salt links with Glu258 or Lys199 of a paramyxovirus HN, which is Newcastle disease virus hemagglutinin neuraminidase. Applying the 3D structure of paramyxovirus HN to design or select a compound involves identifying chemical entities or fragments capable of associating with the enzyme; and assembling the identified chemical entities or fragments into a single molecule to provide the structure of (I).

(M1) employs computational means to perform a fitting operation between (I) and the structure coordinates of the 3D structure; and analyzing the results of the fitting operation to quantify the association between (I) and the structure coordinates.

Preferred Complex: (II) is obtained by diffusion or co-crystallization.

COMPUTING AND CONTROL - Preferred Storage Medium: (III) comprises the 3D structure of Newcastle disease virus HN.

Preferred Computer System: (IV) produces a 3D **representation** of Newcastle disease virus HN and where (III) comprises the structure coordinates of Newcastle disease virus HN.|

AB- <XA> WIDER DISCLOSURE - The following are disclosed:

(1) structure and atomic coordinates of paramyxovirus HN from Newcastle **disease** virus as **determined** by X-ray crystallography;

(2) use of the atomic coordinates for revealing a unique active site which is distinct from other known sialidases or neuraminidases;

(3) structure and atomic coordinates of paramyxovirus HN from Newcastle disease virus co-complex with an inhibitor, 2-deoxy-2,3-dehydro-N-acetylneuraminic acid (DANA) as determined by X-ray crystallography;

(4) use of the atomic coordinates of the co-complex to reveal the active site, and to identify amino acids of the active site that interact with the bound inhibitor;

(5) use of structures of paramyxovirus HN and/or paramyxovirus HN co-complex to solve the structure of HN homologs, mutants, co-complexes and other crystal forms; and

(6) comparison of structures of unbound paramyxovirus HN and co-complex of paramyxovirus HN: DANA as determined by X-ray crystallography, and use of the structures for identifying important amino acids in the active site in the structures.

EXAMPLE - Newcastle disease virus (strain Kanas) was grown in embryonated eggs. The membrane proteins of the virus were isolated by disruption with Triton X-100 and the supernatant containing viral membrane proteins with lipids and Triton X-100 was isolated. Removal of detergent reconstituted the virosomes containing the membrane proteins. Virosomes were then treated with chymotrypsin to cleave hemagglutinin-neuraminidase (HN) from the virosome. A solution containing the cleaved HN was purified by filtration yielding pure concentrated cHN. Crystallization of the cHN was carried out using vapor diffusion in hanging drops. Crystals of cHN belonged to the orthorhombic space group P212121. The unit cell suggested two cHN molecules per asymmetric unit. Brief immersion of the crystals in the crystallization buffer with glycerol added allowed collection of data at 100K. A low resolution phase set was assembled from eight heavy atom derivatives taken at room temperature that gave a mean figure of merit of 0.53 to 4 Angstrom. Attempts to phase extent to 10 Angstrom using

the room temperature native data, NATIVE1 failed to produce an interpretable map. In addition, the non-crystallographic symmetry relating the two cHN molecules could not be **determined** from self rotation **functions** or from native Patterson maps. The structure was finally determined by using the non-isomorphism. Four data sets were chosen that were to as high a resolution possible, were as complete as possible, and were as non-isomorphous from one another as possible. DMMULTI was then used to cross-crystal **average** between the four crystals and to phase extend from 6.0 Angstrom to limits of the individual datasets; using crude masks for each cHN molecule derived by placing a influenza neuraminidase alpha-carbon model roughly into the 4.0 Angstrom MIR map. The resulting electron density allowed rapid tracing of a partial alpha-carbon model for each monomer. These partial models were then used to determine the non-crystallographic symmetry relating the monomers, which was then used in another round of DMMULTI. Interpretation of the structure was carried out using cycles of model building using O (Jones, A.T., Zhou, J.Y., Cowan, S.W. and Kjeldgaard, M. Acta Crystallographica A47:110-119 (1991)) and refinement using CNS (Brunger, A.T. et al., Acta Crystallographica D54:905-921 (1998)). Initially this involved the highest resolution data, NATIVE2, however the refinement did not progress well. All subsequent refinement was carried out using NATIVE3 to 2.5 Angstrom. The final model contained residues 124 to 596 in monomer A residues 124 to 572 in monomer B, one N-linked N-acetylgalactosamine (NAG) at residue 341 in monomer A, two N-linked NAGs at reside 481, a divalent metal (assumed calcium) in monomer A, three glycerol molecules and 211 water molecules. A single binding site on HN provided both the sialic acid binding and hydrolysis functions, and that the functionality appears to be controlled by a conformations switch. There was no evidence for a second sialic acid binding site, as suggested by much of the literature on HN, nor for a site equivalent to the hemagglutinin site found on the neuraminidase of some avian influenza virus strains. The residues interacting with the inhibitor were largely conserved across all HNs of the paramyxoviruses ad suggested that the active site of this Newcastle disease virus HN served as a prototypical model of paramyxovirus HNs. Although the overall gross structure had many similarities with other sialidase/neuraminidases the active site revealed the novel interactions with the substrate that have never before been observed. This suggested that for paramyxovirus HNs, the active site utilized different modes of interaction with substrate in comparison with other neuraminidases such as influenza neuraminidase e.g. in 2-deoxy-2,3-dehydro-N-acetylneuraminic acid (DANA) co-complex there existed interactions with all three hydroxyl groups of the glycerol chain. The compounds which had excellent biological activity toward influenza neuraminidases had little or no biological activity on paramyxovirus HN.|

DE- <TITLE TERMS> IDENTIFY; NEURAMINIDASE; INHIBIT; USEFUL; TREAT; PREVENT; CROUP; APPLY; THREE; DIMENSION; STRUCTURE; ACTIVE; SITE; DESIGN; SELECT ; INHIBIT|

DC- B04; D16|

IC- <MAIN> C12Q-001/70|

IC- <ADDITIONAL> G01N-033/48; G01N-033/50; **G06F-019/00** |

MC- <CPI> B04-L05; B11-C08F3; B11-C08H; B12-K04E; B14-A02B2; B14-C03; B14-K01D; B14-L06; D05-A02C; D05-H09|

FS- CPI||

13/4/4 (Item 4 from file: 350)

DIALOG(R)File 350:Derwent WPIX

IM- *Image available*

AA- 2001-300181/200131|
DX- <RELATED> 2001-281746; 2001-290566|
XR- <XRAM> C01-092144|
XR- <XRPX> N01-215408|
TI- Patient data monitoring system for collecting and providing access to medical data comprises network computer system, patient-specific and condition-specific database, data collectors, communicator, and secure access gateways|
PA- GLAXO GROUP LTD (GLAX)|
AU- <INVENTORS> ANDERSON G J M; BONNEY S G; JONES A P; ROBERTSON D|
NC- 095|
NP- 003|
PN- WO 200126020 A1 20010412 WO 2000EP9292 A 20000922 200131 B|
PN- AU 200077806 A 20010510 AU 200077806 A 20000922 200143
PN- EP 1224600 A1 20020724 EP 2000967752 A 20000922 200256
<AN> WO 2000EP9292 A 20000922|
AN- <LOCAL> WO 2000EP9292 A 20000922; AU 200077806 A 20000922; EP 2000967752 A 20000922; WO 2000EP9292 A 20000922|
AN- <PR> GB 200020541 A 20000822; GB 9923273 A 19991001; GB 200011029 A 20000509|
FD- WO 200126020 A1 G06F-019/00
<DS> (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
<DS> (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
FD- AU 200077806 A G06F-019/00 Based on patent WO 200126020
FD- EP 1224600 A1 G06F-019/00 Based on patent WO 200126020
<DS> (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI|
LA- WO 200126020(E<PG> 55); EP 1224600(E)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW|
DS- <REGIONAL> AL; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LT; LU; LV; MC; MK; NL; PT; RO; SE; SI; EA; GH; GM; KE; LS; MW; MZ; OA; SD; SL; SZ; TZ; UG; ZW|
AB- <PN> WO 200126020 A1|
AB- <NV> NOVELTY - A patient data monitoring system comprises a network computer system; a first patient-specific database and a second condition-specific database; patient electronic data collectors; a communicator; a first secure access gateway that permits access to the first patient- specific database; and a second secure access gateway that permits access to the second condition-specific database.|
AB- <BASIC> DETAILED DESCRIPTION - A patient data monitoring system comprises a network computer system; a first patient-specific database and a second condition-specific database associated with the network computer system; patient electronic data collectors, remote from the network computer system, for collecting patient data relevant to a particular patient's medical condition; a communicator (40), associated with each patient electronic data collector, for communicating with an entry point to the network computer system to enable transfer of the patient data to the first patient-specific database and to the second condition-specific database; a first secure access gateway that permits access to the first patient-specific database in response to a first user authorization command; and a second secure access gateway that permits access to the second condition-specific database in response to a second user authorization command. INDEPENDENT CLAIMS are also included for:

(A) a method for collecting and providing selective user access to

medical data relevant to patients having related medical conditions;

(B) a network computer system for use with the patient data monitoring system; and

(C) a computer program that instructs the computer to perform all the above procedures.

USE - For collecting and providing selective access to medical data relevant to patients having related medical conditions.

ADVANTAGE - The system allows selective monitoring and access to data. It enables patient preferences to be reflected via the use of patient permissions and authorizations. It may also be configured to accommodate situations where the patient waives the right to their control of the collected data by contractual arrangement with the administrators of the system. It also allows availability of information from a remote data source at the initial access point to the network computer system. It allows two-way transfer of data between the network computer and the patient electronic data management system. It further allows integration with a system for electronic prescribing and enables the patient to define permissions or authorizations at the **time** of data collection, data transfer, data storage, and data access. It also allows for remote **assessment** of a patient's **medical condition** and remote prescription.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic **representation** of a system in which a patient electronic data collector forms part of a medicament delivery system.

Communicator (40)

pp; 55 DwgNo 1/11|

AB- <TF> TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Component: The patient data comprises diagnostic data and a compliance data for assessing each patient's compliance with a treatment or prescribing regime. Each patient electronic data collector is under the control of an individual patient and is integrated with a system for the delivery of medicament. The medicament delivery system provides respirable or injectable delivery of medicament to the patient; or is an implant in the body of the patient. The first patient-specific database is separated from, or is a sub-database, to the second condition-specific database. The data within the database is partitioned according to the level of confidentiality or level of commercial sensitivity. The patient electronic data collector further comprises a patient data management system comprising (a) a memory for storage data; a microprocessor for performing operations on the data; (c) a transmitter for transmitting a signal relating to the data or the outcome of an operation on the data; (d) a geographic positioning system; and (e) a data input system. The communicator employs radio frequency or optical signals. It communicates with the network computer system via a telecommunications device comprising a cellular phone or pager.

Preferred Users: The authorized users of the system comprises the patient, a healthcare professional, a pharmacist, an emergency assistance provider, a research professional, and/or a database manager.

Preferred System: The system additionally comprises (a) an authorized user data communicator having the same components as the patient data management system additionally including a communicator; and (b) a display for displaying data from the patient electronic data management system.

Preferred Conditions: The patients have related respiratory conditions or have related cardiovascular conditions.|

DE- <TITLE TERMS> PATIENT; DATA; MONITOR; SYSTEM; COLLECT; ACCESS; MEDICAL; DATA; COMPRISE; NETWORK; COMPUTER; SYSTEM; PATIENT; SPECIFIC; CONDITION ; SPECIFIC; DATABASE; DATA; COLLECT; COMMUNICATE; SECURE; ACCESS; GATEWAY|

DC- B07; S05; T01|

IC- <MAIN> **G06F-019/00** |
IC- <ADDITIONAL> **G06F-001/00** |
MC- <CPI> B11-C03|
MC- <EPI> S05-G02G1; S05-G02G2; S05-M02; T01-J05B4P; T01-J06A1; T01-J12C; T01-S03|
FS- CPI; EPI||

13/4/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX

AA- 2001-244889/200125|
XR- <XRAM> C01-073511|
XR- <XRPX> N01-174359|
TI- Creating a biochemical database for **assessing** a subject's **health** or **medical condition** , comprises compiling biochemical data from thousands of subjects|
PA- LUMINEX CORP (LUMI-N)|
AU- <INVENTORS> CHANDLER M B; CHANDLER V S|
NC- 090|
NP- 002|
PN- WO 200120533 A2 20010322 WO 2000US25183 A 20000915 200125 B|
PN- AU 200075799 A 20010417 AU 200075799 A 20000915 200140|
AN- <LOCAL> WO 2000US25183 A 20000915; AU 200075799 A 20000915|
AN- <PR> US 99153941 P 19990915|
FD- WO 200120533 A2 G06F-019/00
<DS> (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
<DS> (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
FD- AU 200075799 A G06F-019/00 Based on patent WO 200120533|
LA- WO 200120533(E<PG> 25)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW|
DS- <REGIONAL> AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; MZ; NL; OA; PT; SD; SE; SL; SZ; TZ; UG; ZW|
AB- <PN> WO 200120533 A2|
AB- <NV> NOVELTY - Creating a database containing biochemical data from at least 1,000 subjects comprises providing one or more test samples obtained from one or more subjects and exposing a Multi-Analyte **Profile** (MAP) Test Panel to at least a portion of one of the test samples.|
AB- <BASIC> DETAILED DESCRIPTION - Creating a database (I) containing biochemical data from at least 1,000 subjects comprises:

(a) providing one or more test samples obtained from one or more subjects;

(b) exposing a MAP Test Panel to at least a portion of the one or more test samples to provide one or more test mixtures, the MAP Test Panel comprising 20 or more subsets of microspheres, the microsphere of one subset being distinguishable from those of another subset and harboring at least one reagent designed to interact selectively, if not specifically, with and to generate biochemical data concerning a predetermined analyte;

(c) optionally, adding one or more supplemental reagents to the one or more test mixtures to further the generation of the biochemical data;

(d) passing the exposed microspheres of the one or more test

mixtures through a flow analyzer to extract the biochemical data generated;

(e) compiling the biochemical data into a database, which permits retrieval of the biochemical data at least according to the identities or medical histories of the one or more subjects from which the one or more test samples were obtained;

(f) repeating some or all of the foregoing steps until biochemical data from at least 1,000 subjects are compiled into the database.

INDEPENDENT CLAIMS are also included for the following:

(1) a Multi-Analyte **Profile** (MAP) Test Panel comprising 20 or more subsets of microspheres, the microspheres of one subset being distinguishable from those of another subset and harboring at least one reagent designed to interact selectively, if not specifically with a predetermined analyte;

(2) a kit for assaying 20 or more predetermined analytes in a single pass through a flow analyzer comprising a MAP Test Panel comprising 20 or more subsets of microspheres;

(3) a method (II) of **assessing** a subject's **health** or **medical condition** comprising:

(a) providing one or more test samples obtained from a subject; and

(b) exposing the one or more test samples to a MAP Test Panel;

(c) gathering the biochemical data generated from the exposure;

(d) comparing the biochemical data generated from the one or more samples obtained from the subject with accumulated biochemical data generated form test samples taken periodically from at least 1,000 individuals over a given **time** interval, which accumulated biochemical data provide a relationship between one or more predetermined analytes and the health or medical condition of a number of individuals whose accumulated biochemical data share similar features; and

(e) **assessing** the **health** or **medical condition** of the subject on the results of the comparison;

USE - The method is useful for creating a database containing biochemical data, including details from physical, medical or psychiatric examinations and medical histories of 5,000-100,000 subjects, which can be used in an **assessment** of a subject's **health** or **medical condition** (claimed).

ADVANTAGE - The novel method provides a data base of biochemical data from test samples obtained from up to 100,000 subjects, which is used to create a computerized model of normal, healthy biology, then through the analysis of further test samples obtained from subjects in the midst of a diseased state, the invention models the chain of protein events that cause the disease to occur. Previous methods in comparison, only gave a vague picture of the elements of a healthy lifestyle, correlation between genetic and environmental factors and a particular disease.

pp; 25 DwgNo 0/0|

AB- <TF> TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred MAP Test Panel: The panel comprises between 50-300 or more subsets of microspheres, one subset is distinguishable from those of another by their characteristic fluorescence signatures, a variety of concentrations of two or more fluorescent dyes are contained within the microspheres. The reagents comprises a small molecule, natural product, synthetic polymer, peptide, polypeptide, polysaccharide, lipid, nucleic acid or a combination of these, the predetermined analyte comprises a drug, hormone, antigen, antibody, protein, enzyme, DNA, RNA or a combination of these.

Preferred Method: In method (I) one or more of the test samples comprises biological fluids, mixtures or preparations of these, specifically blood samples or mixtures, which are obtained from between 5,000-100,000 subjects at least every month, quarter, biannually or annually or over a period of 3-9 years. The biochemical data includes information concerning the presence, absence or quantity of 20 or more

predetermined analytes present in the test samples, in which some or all of the subjects suffer from good or poor health, or have been diagnosed with a disease or other pathological condition, for example a neoplastic, neurodegenerative, skeletal, muscular, connective tissue, skin, organ, metabolic, addictive or psychiatric disease. The subjects may also be subjected to a physical, medical or psychiatric examination, requested to fill out a questionnaire or provide details of their medical histories, in some cases subjects are examined and questioned, have their biochemical data assessed and their medical histories determined annually over the same period. Relationships are determined between the changes in the biochemical data and the changes in the medical conditions or histories of the subjects, which can provide evidence that changes in the biochemical data correlate, are predictive or even cause one or more changes in the medical conditions or histories. One or more supplemental reagents comprises a substrate, antibody, protein, enzyme, DNA, RNA or combinations of these. The exposed microspheres from the test mixtures is filtered prior to passing the filtered microspheres through the flow analyzer.

In method (II) the **time** interval is as long as 3-5 years.|

AB- <XA> WIDER DISCLOSURE - Also disclosed as new are the following:

(1) an algorithm for **predicting** a **disease** in a subject comprising mathematics and statistics for evaluating information on protein levels and an output **predictive** of **disease** ;

(2) a system for **predicting** a **disease** ;

(3) a method for developing a mathematical model **predictive** of **disease** ; and

(4) a method for treating a disease.

EXAMPLE - No suitable examples are provided|

DE- <TITLE TERMS> BIOCHEMICAL; DATABASE; ASSESS; SUBJECT; HEALTH; MEDICAL; CONDITION; COMPRISE; COMPILE; BIOCHEMICAL; DATA; THOUSAND; SUBJECT|

DC- B04; D16; T01|

IC- <MAIN> **G06F-019/00** |

MC- <CPI> B11-C08C; B11-C08E2; B12-K04A; D05-H09; D05-H10; D05-H13|

MC- <EPI> T01-J|

FS- CPI; EPI||

13/4/6 (Item 6 from file: 350)

DIALOG(R)File 350:Derwent WPIX

IM- *Image available*

AA- 1992-375000/199246|

XR- <XRPX> N92-285855|

TI- Electrical signal processing system for electrocardiographic use - uses 12 lead **set** providing **data** which is transformed to produce spatial **distribution** representative of 192 lead **set** **data** |

PA- PHYSIO CONTROL CORP (PHYS-N); PHYSIO-CONTROL (PHYS-N)|

AU- <INVENTORS> EVANS A K; MERCHANT M H|

NC- 020|

NP- 010|

PN- EP 512719 A2 19921111 EP 92303703 A 19920424 199246 B|

PN- US 5161539 A 19921110 US 91697332 A 19910509 199248

PN- AU 9214893 A 19921112 AU 9214893 A 19920414 199301

PN- CA 2066080 A 19921110 CA 2066080 A 19920415 199305

PN- EP 512719 A3 19921125 EP 92303703 A 19920424 199343

PN- US 5318037 A 19940607 US 91697332 A 19910509 199422

<AN> US 92944398 A 19921013

PN- US 5377687 A 19950103 US 91697332 A 19910509 199507

<AN> US 92944398 A 19921013

<AN> US 94196019 A 19940214

PN- EP 512719 B1 19970122 EP 92303703 A 19920424 199709

PN- DE 69216904 E 19970306 DE 616904 A 19920424 199715
<AN> EP 92303703 A 19920424
PN- JP 3242981 B2 20011225 JP 92114764 A 19920507 200203|
AN- <LOCAL> EP 92303703 A 19920424; US 91697332 A 19910509; AU 9214893 A 19920414; CA 2066080 A 19920415; EP 92303703 A 19920424; US 91697332 A 19910509; US 92944398 A 19921013; US 91697332 A 19910509; US 92944398 A 19921013; US 94196019 A 19940214; EP 92303703 A 19920424; DE 616904 A 19920424; EP 92303703 A 19920424; JP 92114764 A 19920507|
AN- <PR> US 91697332 A 19910509; US 92944398 A 19921013; US 94196019 A 19940214|
CT- No-SR.Pub; 4.Jnl.Ref|
FD- EP 512719 A2 A61B-005/0408
<DS> (Regional): AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE
FD- US 5318037 A A61B-005/0452 Cont of application US 91697332
Cont of patent US 5161539
FD- US 5377687 A A61B-005/452 Cont of application US 91697332
Cont of application US 92944398
Cont of patent US 5161539
Cont of patent US 5318037
FD- EP 512719 B1 A61B-005/0408
<DS> (Regional): AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE
FD- DE 69216904 E A61B-005/0408 Based on patent EP 512719
FD- JP 3242981 B2 A61B-005/0452 Previous Publ. patent JP 6125883|
LA- EP 512719(E<PG> 27); US 5161539(23); US 5318037(22); US 5377687(22); EP 512719(E<PG> 25); JP 3242981(23)|
DS- <REGIONAL> AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; PT; SE|
AB- <BASIC> EP 512719 A

The body electrical signal processing system uses a 12-lead electrocardiographic set using a single 10-electrode cable set. The monitor (16) receives nine leads of data from the electrode cable set and initially preprocesses it to simplify further analysis.

The data from the patient is then transformed to produce a spatial **distribution** relative to the patients chest which is representative of the data which would be collected by a 192 electrode **set** . **Feature** extraction is applied to statistically analysed to detect cardiac conditions.

ADVANTAGE - Provides spatial distributions without complex electrode configurations. Increased analytical capability.

Dwg.2/10|

AB- <EP> EP 512719 B

A system for **determining** whether a patient has a coronary **disease** , comprising: a first set of electrodes (L, R, R, G, p1, p2, p3, p4, p5, p6) for receiving a first set of cardiac signals from a patient, at less than twenty electrodes; a data conversion interface (30) connected to receive the first set of cardiac signals and to convert the first set of cardiac signals into a digital form; memory means (34) for storing a **function** that **computes** a canonical variable using three or more statistically determined coefficients taken from a set of coefficients; a central processing unit (32) that is programmed to: a) transform the digitised set of cardiac signals into a greater number of digitised values, the set of values representing a set of body surface mapping signals such that the first set of cardiac signals appear as if they had been received from the patient using a set of body surface mapping electrodes, at more than twenty electrodes, and the body surface mapping electrodes had received the whole set of body surface mapping signals; the transformation using a mathematical expectation operator and stored referential data; b) to expand the transformed set of values representing the body surface mapping signals as a linear combination of predetermined spatial basis **functions** to **determine** the set of coefficients as being the coefficients of the linear expansion; c) to compute a value for the

canonical variable using the stored function; and d) to compare the value of the canonical variable to a cut point above which the canonical variable indicates that the patient has the coronary disease and below which the canonical variable indicates the patient does not have the disease; and a display (38) that indicates whether the patient has the coronary disease, the display being activated by the central processing unit if the value of the value of the canonical variable is greater than the cut point.

Dwg.1/10|

AB- <US> US 5377687 A

The appts. for coronary monitoring includes a monitor for use in performing 12-lead electrocardiographic and body surface mapping analyses on a patient with a single ten-electrode cable set. The monitor receives nine leads of data from the electrode cable set and initially pre-processes it to simplify further analysis. The data is transformed to produce a spatial **distribution** relative to the patient's chest, representative of the data that would be collectible with an electrode set.

Feature extraction techniques are used for evaluating transformed, as well as conventional, BSM data with respect to clinically evaluated populations. In that regard, features of interest are extracted from the data and statistically analysed to detect select cardiac conditions.

USE - Monitoring and analysis of the electrical activity of, for example, a patient's heart and, more particularly to monitoring and analysis of the spatial **distribution** of the electrical activity, based upon, for example, information collected from a limited number of electrodes.

Dwg.1/10

US 5161539 A

The (10) includes a monitor (16) for use in performing 12-lead electrocardiographic (ECG) and body surface mapping (BSM) analyses on a patient (12) with a single ten-electrode cable set (14). The monitor receives none leads of data from the electrode cable set and initially preprocesses it to simplify further analysis. Then the data is transformed to produce a spatial **distribution** relative to the patient's chest, representative of the data that would be collectible with a 192-electrode set.

Feature extraction techniques are used in evaluating transformed, as well as convenient, BSM data with respect to clinically evaluated populations. In that regard, features of interest are extracted from the data and statistically analysed to detect select cardiac conditions.

Dwg.1/10

US 5318037 A

The system for receiving a first set of electrical signals from a patient at less then twenty electrodes to obtain information that is conventionally available from a second set of electrical signals collected from a greater number of electrodes comprises transformation unit for receiving the first set of electrical signals and for performing a linear transformation upon the first set of electrical signals, using a least-square approximation, to generate a transformed vector **representation** of a map-type data set that is itself representative of the second set of electrical signals.

It has an extraction unit for extracting at least one feature from the map-type data set. Non-cardiac elements may influence the transformed vector and the transformation unit further comprises normalisation means for normalising the transformed vector to reduce the influence of non-cardiac elements on the transformed vector.

USE - To monitor and analyse electrical activity of for example, patients heart.

Dwg.1/11|
DE- <TITLE TERMS> ELECTRIC; SIGNAL; PROCESS; SYSTEM; ECG; LEAD; SET; DATA; TRANSFORM; PRODUCE; SPACE; DISTRIBUTE; REPRESENT; LEAD; SET; DATA|
DE- <ADDITIONAL WORDS> MEDICAL; BODY; SURFACE; MAPPING|
DC- P31; S05|
IC- <MAIN> A61B-005/04; A61B-005/0402; A61B-005/0408; A61B-005/045; A61B-005/0452; A61B-005/452|
IC- <ADDITIONAL> A61B-005/0205; A61B-005/0428; **G06F-015/42** ; **G06F-019/00** |
MC- <EPI> S05-A02; S05-D01A1|
FS- EPI; EngPI||

13/4/7 (Item 1 from file: 347)
FN- DIALOG(R)File 347:JAPIO|
CZ- (c) 2002 JPO & JAPIO. All rts. reserv.|
TI- DIAGNOSING METHOD OF DISEASE CONDITION
PN- 58-178481 -JP 58178481 A-
PD- October 19, 1983 (19831019)
AU- MIURA JUNKICHI; TAKADA YOSHITADA; MIYAGI HIROYUKI; TAKI MAMORU; YAMAGATA AKIRA
PA- HITACHI LTD [000510] (A Japanese Company or Corporation), JP (Japan)
AN- 57-061012 -JP 8261012-
AN- 57-061012 -JP 8261012-
AD- April 14, 1982 (19820414)
IC- -3- **G06F-015/42** ; A61B-005/00; G01N-031/08; G01N-033/48
CL- 45.4 (INFORMATION PROCESSING -- Computer Applications); 28.2 (SANITATION -- Medical); 46.2 (INSTRUMENTATION -- Testing)
KW- R115 (X-RAY APPLICATIONS); R131 (INFORMATION PROCESSING -- Microcomputers & Microprocessers)
SO- Section: P, Section No. 251, Vol. 08, No. 23, Pg. 45, January 31, 1984 (19840131)
AB- PURPOSE: To decide on a **disease** and its **condition** uniformly, by **analyzing** urine with chromatography, and dividing plural specific analyzed components by the amount of components having some community of analytic results and obtaining multidimensional **representation** .

CONSTITUTION: Sample urine to be analyzed is contained in test tubes set on the turntable 2 of an automatic sampler 1. An eluent in a regent bottles 10A is flowed into separating columns 13 and 14, whose contents are placed in a equilibrium state. The sample urine in the turntable 2 is held in a sampling coil 4 a specific **time** after an analyzer is driven. Then, an injector 3 rotates to allow the sample urine to enter the separating columns 13 and 14 together with the elent. Separated components from the separating columns 13 and 14 are supplied to an U-V monitor 17, where they are analyzed. The analytic result is divided by the amount of components having some community of the analytic result to make an accurate decision.
?

?t14/ti/all

14/TI/1 (Item 1 from file: 350)

Determining single nucleotide polymorphisms in nucleotide sequence of preselected gene, comprises isolating fragment of preselected gene from each individual of random population and identifying single nucleotide polymorphism

14/TI/2 (Item 2 from file: 350)

System for dispensing nanoliter sized droplets in defined distribution **pattern to form miniarrays comprises print head with pipette-based dispensers, robotic arm for carrying print head and working platform**

14/TI/3 (Item 3 from file: 350)

Farm management system for animals, has computer which compares measured milk flow profile **of animal with stored reference milk flow** profiles **for identification of animal**

14/TI/4 (Item 4 from file: 350)

Detection and interpretation of mutations through expression or function tests **of haploid genes, useful for detecting e.g. loss-of-function or gain-of-function mutations**

14/TI/5 (Item 5 from file: 350)

New non-genetic based protein disease markers for obesity, osteoporosis, diabetes, osteoathritis and hypertension, useful in diagnosis and monitoring of treatment for these diseases and to screen for therapeutic compounds

14/TI/6 (Item 6 from file: 350)

Internal biological **tissue** condition **characterization for human/animal body, involves** estimating **statistical measure of coefficient** distribution **of wavelet maxima** representation **of segmented digital images, in spectral band**

14/TI/7 (Item 7 from file: 350)

Novel microtubule motor protein for screening modulators of HsKip3d, useful in treatment of hyperproliferative disease e.g. cancer, autoimmune disease, arthritis, graft rejection, inflammatory bowel disease

14/TI/8 (Item 8 from file: 350)

Novel isolated Helicobacter pylori heptosyltransferase polypeptides (WaaF and WaaC) and polynucleotides encoding the polypeptides, useful to identify antibacterial compounds which modulate heptosyltransferase activity

14/TI/9 (Item 9 from file: 350)

Novel Helicobacter pylori DD-heptosyl transferase polypeptide and polynucleotide, useful for treating diseases associated with Helicobacter pylori infection e.g. gastric ulcer and gastritis

14/TI/10 (Item 10 from file: 350)

Determining presence of specific nucleotide sequence in RNA reagent of sample by using a capture reagent having a label and a nucleotide sequence complementary to capture sequence attached to RNA reagent on microarray

14/TI/11 (Item 11 from file: 350)

Five novel proteins, termed KIA0301, G7c, KIAA0564, CAB01991.1 and Rv0368c, which have been identified as adhesion molecules, useful in the treatment and diagnosis of disease such as a cardiovascular disease, cancer and immune disorders

14/TI/12 (Item 12 from file: 350)

Screening a subject for Alzheimer's disease (AD) by detecting presence of a marker associated with gene linked to AD, which indicates that the subject is afflicted with or is at risk of developing AD

14/TI/13 (Item 13 from file: 350)

Measurement of subject's working memory for determining **overall cognitive** ability **, involves presenting attention-demanding task and** measuring **subject's behavioral responses to the task and neuroelectric activity**

14/TI/14 (Item 14 from file: 350)

New genetic variants of human hydroxy- delta **-5-steroid dehydrogenase, 3 beta- and steroid** delta **-isomerase 1 gene for expressing protein for use in screening for drugs to treat steroid biosynthesis disorders**

14/TI/15 (Item 15 from file: 350)

Existence of an alternate glucose pathway for treating mental and neurological disorders is proved by considering cerebral spinal fluid as the major component

14/TI/16 (Item 16 from file: 350)

Method for disease diagnosis comprises comparing a test **sample with reference samples for known** diseases **that are similar to the** test **sample in physiological state**

14/TI/17 (Item 17 from file: 350)

Deciphering genetic function, useful to find new therapeutic targets and to evaluate candidate drugs, comprises analyzing treatment response of a matrix of parent and target specific modified cell lines

14/TI/18 (Item 18 from file: 350)

Assessing status of cellular pathway such as cell growth, cell death pathway, by applying cell lysate containing cellular pathway molecules to immobilized series of binding reagents which discriminate the molecules

14/TI/19 (Item 19 from file: 350)

Method for analyzing gene expression, comprises multiplex amplifying target cDNA sequences using target-specific and universal primers, generating gene expression data and comparing with other gene expression data

14/TI/20 (Item 20 from file: 350)

Determining the presence of atherosclerosis, preferably coronary artery disease **or susceptibility comprises** determining **the CA repeat number in intron 13 of the endothelial nitric oxide synthase gene**

14/TI/21 (Item 21 from file: 350)

Generating oligonucleotides, involves ligating a double-stranded DNA to another dsDNA comprising IIS restriction endonuclease recognition site, restricting ligated dsDNA, and detecting IIS-restricted dsDNA

14/TI/22 (Item 22 from file: 350)

Health profiling **of animals e.g. horses, by combining genetic data of animals with health** assessment **data to permit** analysis predicting health , disease , **disorder probabilities and longevity of animals**

14/TI/23 (Item 23 from file: 350)

Evaluating **a** biological condition **of a subject, involves deriving first** profile **data set from patient sample for quantitative measure of RNA or protein in a panel and producing calibrated** profile **data set for panel**

14/TI/24 (Item 24 from file: 350)

Human leukocyte antigen typing by amplifying a sample followed by sequence specific oligonucleotide hybridization with labeled oligonucleotide probes that hybridize with a series of known control DNA sequences

14/TI/25 (Item 25 from file: 350)

Evaluating the toxicity of a compound comprises observing the intracellular localization of a signal transduction protein in the presence and absence of the candidate compound

14/TI/26 (Item 26 from file: 350)

Cardiopulmonary exercise testing apparatus uses test station with gas analyzers, flow measurement means and compression bottle, used to predict **future health of coronary artery** disease **sufferers**

14/TI/27 (Item 27 from file: 350)

Assessing risk of developing Type 2 diabetes or insulin resistance using NMR measurements of lipoproteins and, optionally, glucose levels, allows early detection

14/TI/28 (Item 28 from file: 350)

Partitioning polymorphic DNA molecules useful for designing assays for determining **identity, ancestry, predisposition to** disease **or presence of a desired** trait **, gene mapping and drug development, by graph coloring technique**

14/TI/29 (Item 29 from file: 350)

Detection of the presence of or risk of developing a condition or disorder involving cellular abnormalities such as thrombosis and heart disease **comprises** determining **binding** capacity **of cells in sample**

14/TI/30 (Item 30 from file: 350)

Measuring in vivo complement activation of lectin pathway in mammals includes obtaining plasma sample with metal ion chelator that binds calcium ions and measuring kinetics of in vitro activation

14/TI/31 (Item 31 from file: 350)

Controlled administration of testosterone, e.g. for hormone replacement therapy, using buccal bioadhesive system containing testosterone ester(s) to give targeted release profile
?

?t14/4/6,13,16,22,23,

14/4/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

IM- *Image available*
AA- 2002-329178/200236|
DX- <RELATED> 1998-480862; 2001-624364; 2002-204550|
XR- <XRPX> N02-258394|
TI- Internal **biological** tissue **condition** characterization for human/animal body, involves **estimating** statistical measure of coefficient **distribution** of wavelet maxima **representation** of segmented digital images, in spectral band|
PA- ELECTRO-OPTICAL SCI INC (ELEC-N)|
AU- <INVENTORS> BOGDAN A; ELBAUM M; GREENEBAUM M; GUTKOWICZ-KRUSIN D; JACOBS A|
NC- 094|
NP- 002|
PN- WO 200201143 A2 20020103 WO 2001US20524 A 20010627 200236 B|
PN- AU 200170220 A 20020108 AU 200170220 A 20010627 200236|
AN- <LOCAL> WO 2001US20524 A 20010627; AU 200170220 A 20010627|
AN- <PR> US 2000604645 A 20000627|
FD- WO 200201143 A2 G01B-000/00
<DS> (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
<DS> (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
FD- AU 200170220 A G01B-000/00 Based on patent WO 200201143|
LA- WO 200201143(E<PG> 12)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW|
DS- <REGIONAL> AT; BE; CH; CY; DE; DK; EA; ES; FI; FR; GB; GH; GM; GR; IE; IT; KE; LS; LU; MC; MW; MZ; NL; OA; PT; SD; SE; SL; SZ; TR; TZ; UG; ZW|
AB- <PN> WO 200201143 A2|
AB- <NV> NOVELTY - Light image of a specific region of the tissue (22), transmitted to a receiver is segmented into multiple signals by generating a mask defining the boundary of desired region of the tissue in a specified spectral band. The rotationally and translationally invariant statistical measure of the coefficient distributions of the multiscale wavelet maxima representations of the images, are **estimated** in each band, to characterize tissue **condition** . |
AB- <BASIC> DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for internal biological tissue condition characterizing system.
USE - For classification of biological tissue of stomach, esophagus, colon or nasal cavities in human or animal body.
ADVANTAGE - Enables automatically characterizing biological tissues effectively.
DESCRIPTION OF DRAWING(S) - The figure shows the articulated arm of biological tissue characterizing system.
Tissue (22)
pp; 12 DwgNo 2/2|
DE- <TITLE TERMS> INTERNAL; BIOLOGICAL; TISSUE; CONDITION; CHARACTERISTIC; HUMAN; ANIMAL; BODY; ESTIMATE; STATISTICAL; MEASURE; COEFFICIENT; DISTRIBUTE; MAXIMUM; REPRESENT; SEGMENT; DIGITAL; IMAGE; SPECTRAL; BAND |
DC- S03; S05|
IC- <MAIN> G01B-000/00|

MC- <EPI> S03-E04C; S03-E04X; S05-D01J; S05-D02X|
FS- EPI||

14/4/13 (Item 13 from file: 350)
DIALOG(R)File 350:Derwent WPIX

AA- 2002-130826/200217|
XR- <XRAM> C02-040206|
XR- <XRPX> N02-098673|
TI- Measurement of subject's working memory for **determining** overall cognitive **ability** , involves presenting attention-demanding task and **measuring** subject's behavioral responses to the task and neuroelectric activity|
PA- SAM TECHNOLOGY INC (SAMT-N)|
AU- <INVENTORS> GEVINS A S; SMITH M E|
NC- 022|
NP- 002|
PN- WO 200200110 A1 20020103 WO 2001US19600 A 20010620 200217 B|
PN- US 6434419 B1 20020813 US 2000603218 A 20000626 200255|
AN- <LOCAL> WO 2001US19600 A 20010620; US 2000603218 A 20000626|
AN- <PR> US 2000603218 A 20000626|
FD- WO 200200110 A1 A61B-005/00
<DS> (National): CA JP
<DS> (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR|
LA- WO 200200110(E<PG> 63)|
DS- <NATIONAL> CA JP|
DS- <REGIONAL> AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR|
AB- <PN> WO 200200110 A1|
AB- <NV> NOVELTY - A subject's working memory is measured by presenting an attention-demanding task to the subject. The subject's behavioral responses to the task and neuroelectric activity are measured using a set of electroencephalograph electrodes, amplifier and analog/digital converters to provide a **set** of digital **data** representing the subject's behavioral responses and neuroelectric activity.|
AB- <BASIC> DETAILED DESCRIPTION - Measurement of a subject's working memory involves:

(a) presenting an attention-demanding task that engages the working memory processes, to the subject;

(b) measuring the subject's behavioral responses to the task and neuroelectric activity using a set of electroencephalograph (ECG) electrodes, amplifier and analog/digital converters to provide a **set** of digital **data** representing the subject's behavioral responses and neuroelectric activity in response to the task;

(c) comparing the digital data representing behavioral responses and neuroelectric activity in response to the task to a **set** of digital **data** representing the behavioral responses and EEG derived neuroelectric responses of a normal group to the same task, using a computer system; and

(d) displaying the subject's overall cognitive ability score(s) based on the comparison with the normal group.

USE - The method is for measuring a subject's working memory to **determine** the subject's overall cognitive **ability** (i.e., general intelligence).

ADVANTAGE - The inventive method **measures** overall cognitive **ability** quickly, objectively, inexpensively, and with minimal cultural bias. It allows for **measurement** of changes due to **diseases** , injury, fatigue, or treatment with drugs or other remedial therapies. It improves brain function or reduces the progression of diseases or

conditions that affect higher cognitive brain functions.
pp; 63 DwgNo 0/14|
AB- <TF> TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Method: A passive control condition is presented to the subject for comparison to the attention-demanding task. The subject's neuroelectric activity is measured while performing the attention-demanding task to **determine** the subject's **level** of alertness, mental efforts and brain utilization, sustained focused attention, neurocognitive strategy, cognitive speed, transient focused attention, how the brain and behavior respond to changes in mental workload, and the subject's quickness to adapt. The **level** of alertness is characterized by EEG **measurement** of the frontal **delta** **power** associated with slow horizontal eye movements, posterior theta and **delta** power, and ratios of posterior theta to alpha and **delta** to alpha powers. The mental efforts and brain utilization are characterized by EEG measurement of parietal and prefrontal alpha powers. The sustained focused attention is characterized by EEG **measurement** of frontal midline theta **power** . The neurocognitive strategy is characterized by EEG measurement of left to right and anterior to posterior ratios of alpha powers. The cognitive speed is characterized by EEG measurement of fronto-central P200 and P300 evoked potential peak latencies. The transient focused attention is characterized by EEG measurement of fronto-central P200 and P300 evoked potential amplitudes. The manner on how the brain and behavior respond to changes in mental workload is characterized by presenting more and less difficult versions of the same task during the same test session and measuring differences between the difficulty levels. The subject's quickness to adapt is characterized by measuring changes in the neutral activity as the subject continues to perform the attention demanding tasks during the same test session. The method may be performed several times to obtain prior set of cognitive ability scores and subsequent cognitive scores. The subsequent cognitive ability scores are then compared to the prior set of scores.|
DE- <TITLE TERMS> MEASURE; SUBJECT; WORK; MEMORY; DETERMINE; OVERALL; COGNITIVE; ABILITY; PRESENT; ATTENTION; DEMAND; TASK; MEASURE; SUBJECT; BEHAVE; RESPOND; TASK; ACTIVE|
DC- B04; P31; S05|
IC- <MAIN> A61B-005/00|
MC- <CPI> B11-C08; B12-K04C|
MC- <EPI> S05-D01D|
FS- CPI; EPI; EngPI||

14/4/16 (Item 16 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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AA- 2002-025586/200203|
XR- <XRAM> C02-007015|
TI- Method for disease diagnosis comprises comparing a **test** sample with reference samples for known **diseases** that are similar to the **test** sample in physiological state|
PA- MAHADEVAPPA M (MAHA-I); WARRINGTON J A (WARR-I)|
AU- <INVENTORS> MAHADEVAPPA M; WARRINGTON J A|
NC- 001|
NP- 001|
PN- US 20010044104 A1 20011122 US 2000193719 A 20000331 200203 B
<AN> US 2000231367 A 20000908
<AN> US 2000240678 A 20001013
<AN> US 2000734752 A 20001211|
AN- <LOCAL> US 2000193719 A 20000331; US 2000231367 A 20000908; US 2000240678 A 20001013; US 2000734752 A 20001211|
AN- <PR> US 2000734752 A 20001211; US 2000193719 P 20000331; US 2000231367

P 20000908; US 2000240678 P 20001013|
FD- US 20010044104 A1 C12Q-001/68 Provisional application US 2000193719
Provisional application US 2000231367
Provisional application US 2000240678|
LA- US 20010044104(16)|
AB- <PN> US 20010044104 A1|
AB- <NV> NOVELTY - Disease diagnosis comprises:
(a) measuring the physiological state of a test sample;
(b) selecting reference samples for known **diseases** that are similar to the **test** sample in physiological state; and
(c) comparing the test and reference samples to identify a reference sample that matches the test sample|
AB- <BASIC> DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) disease diagnosis comprising:
(a) measuring the physiological state of a test sample;
(b) selecting reference samples for known **diseases** that are similar to the **test** sample in physiological state; and
(c) comparing the expression **profiles** of the test and reference samples to identify a reference sample that matches the test sample;
(2) identifying markers to assay the **efficacy** of drug therapies in women, comprising **measuring** the expression **profile** of a sample from a female subject before drug treatment and comparing it with the expression **profile** of a sample from the same subject after drug treatment;
(3) diagnosing physiological disorders, comprising comparing a gene expression **profile** from a test sample with a gene expression **profile** that represents an **average** of several reference samples with matching indicators of physiological status;
(4) identifying the physiological status of a sample of unknown origin, comprising generating an expression **profile** from the sample and comparing the expression **profile** with expression **profiles** of known physiological states;
(5) identifying markers of different physiological states in humans, comprising:
(a) matching a sample from a first physiological state to a sample from a second physiological state;
(b) comparing the expression **profiles** from the first and second physiological states; and
(c) identifying genes that are differentially expressed in the first and second physiological states.
USE - The method is used for disease diagnosis, e.g. by comparing a sample from a 30-year-old female having difficulty in becoming pregnant with samples from 30-year-old females diagnosed with specific forms of infertility.
pp; 16 DwgNo 0/0|
AB- <TF> TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The samples in (5) are matched according to pharmacological and/or disease state.|
AB- <XA> EXAMPLE - No relevant examples are given.|
DE- <TITLE TERMS> METHOD; DISEASE; DIAGNOSE; COMPRISE; COMPARE; TEST; SAMPLE; REFERENCE; SAMPLE; DISEASE; SIMILAR; TEST; SAMPLE; PHYSIOLOGICAL; STATE|
DC- B04; D16|
IC- <MAIN> C12Q-001/68|
MC- <CPI> B04-E03; B11-C08E; B11-C08F; B12-K04A; B12-K04E; B12-K04F; D05-H09|
FS- CPI||

14/4/22 (Item 22 from file: 350)
DIALOG(R)File 350:Derwent WPIX

AA- 2001-407932/200143|
XR- <XRAM> C01-123481|
XR- <XRPX> N01-301854|
TI- Health **profiling** of animals e.g. horses, by combining genetic data of animals with health **assessment** data to permit **analysis predicting health , disease** , disorder probabilities and longevity of animals|
PA- DODDS W J (DODD-I)|
AU- <INVENTORS> DODDS W J|
NC- 095|
NP- 005|
PN- WO 200128415 A1 20010426 WO 2000US25924 A 20000922 200143 B|
PN- AU 200078308 A 20010430 AU 200078308 A 20000922 200148
PN- US 6287254 B1 20010911 US 99432851 A 19991102 200154
PN- US 20020022772 A1 20020221 US 99432851 A 19991102 200221
<AN> US 2001908407 A 20010822
PN- EP 1223852 A1 20020724 EP 2000968382 A 20000922 200256
<AN> WO 2000US25924 A 20000922|
AN- <LOCAL> WO 2000US25924 A 20000922; AU 200078308 A 20000922; US 99432851 A 19991102; US 99432851 A 19991102; US 2001908407 A 20010822; EP 2000968382 A 20000922; WO 2000US25924 A 20000922|
AN- <PR> US 99432851 A 19991102; US 99419192 A 19991015; US 2001908407 A 20010822|
FD- WO 200128415 A1 A61B-005/00
<DS> (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
<DS> (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
FD- AU 200078308 A A61B-005/00 Based on patent WO 200128415
FD- US 20020022772 A1 A61B-005/00 Cont of application US 99432851
Cont of patent US 6287254
FD- EP 1223852 A1 A61B-005/00 Based on patent WO 200128415
<DS> (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI|
LA- WO 200128415(E<PG> 43); EP 1223852(E)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW|
DS- <REGIONAL> AL; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LT; LU; LV; MC; MK; NL; PT; RO; SE; SI; EA; GH; GM; KE; LS; MW; MZ; OA; SD; SL; SZ; TZ; UG; ZW|
AB- <PN> WO 200128415 A1|
AB- <NV> NOVELTY - Health **profiling** of an animal involves obtaining genetic data of the animal and health assessment data of the animal; combining this data with data relating to or **assessing diseases** , disorders and physiologic states of the animal; and producing a report from these data. The report includes **evaluation** of **health , disease** and disorder probabilities and longevity of the animal.|
AB- <BASIC> DETAILED DESCRIPTION - Health **profiling** of an animal involves (a) obtaining genetic data of the animal and health assessment data of the animal; (b) combining this data with the neurotransmitter data relating to the temperament and longevity of the animal, data assessing the bodily fluid and tissue immune stimulation reaction, (para)neoplastic change or cellular inflammatory response of the animal, metabolic marker of the animal for inherited organ dysfunction or dysplasia, a physiologic or genetic marker for autoimmune thyroiditis, data assessing the presence of or susceptibility to mammary cancer of the animal, data assessing the integrity of immune surveillance mechanisms of the animal, and/or data **assessing** the risk

of inherited bleeding **disease** or disorder of the animal; and (c) producing a report from these data. The report includes **evaluation** of **health** , **disease** and disorder probabilities and longevity of the animal.

INDEPENDENT CLAIMS are also included for:

(1) a method of communicating data related to the animal, involving receiving an access request message from a remote user via a communications link, transmitting an access enabling message to the user via the communications link, compiling a report including health assessment and genetic data related to the animal from an accessed database, and transmitting the compiled report to the remote user;

(2) a method of analyzing, using a computer, the phenotypic and genotypic data based on predetermined characteristics and reporting the analysis of the combined phenotypic and genotypic data;

(3) an apparatus for communicating data related to the animal including a computer communication network for data communication between a central database processing resource and remote user(s), mechanism for receiving an access request message from a remote user via the communications link, mechanism for transmitting an access, mechanism for compiling a report from the accessed database, and communication network transmitting the compiled report of the health assessment and genetic data of the animal to the user;

(4) a computer-readable medium including instructions to access data on the medium, a database medium related to the genotypic data of an animal, and a database on the medium related to the phenotypic data of the animal; and

(5) a system for reporting the analysis of the combined phenotypic and genotypic data, including (a) a computer based communications network, (b) a computer at a central database processing resource provider for receiving the phenotypic data including physical and health assessment data and genotypic data including genetic background, genomic mapping and genetic screening data, (c) screen for monitoring the phenotypic and genotypic data, (d) computer for analyzing the phenotypic and genotypic data based on predetermined characteristics, and (e) computer for receiving, through the network, the analysis.

USE - The method is for **testing** , diagnosis and **prediction** of **diseases** and disorders of companion animals, sports animals, farm animals such as dogs, cats, horses, cows, swine, goats and zoo animals. It is further used for reducing morbidity and mortality of animals, and for improving the quality of their life and their lifespan.

ADVANTAGE - The method stores and/or presents both phenotypic information and genotypic information as a comprehensive and cumulative assessment of individual animals or group of animals. The present system for inputting, storing and retrieving data related to animal health assessment and genetics permits effective use of the health **profile** of the animal. It provides enough data to correctly diagnose and predict disorders.

pp; 43 DwgNo 0/8|

AB- <TF> TECHNOLOGY FOCUS - BIOLOGY - Preferred Data: The following characteristics are determined: (A) the temperament of the animal which involves obtaining data related to the value of serotonin, gamma-aminobutyric acid, glutamate, dopamine, glycine, aspartate, acetylcholine, norepinephrine, histamine, substance P, vasopressin, vasoactive intestinal peptide, neurotensin, and/or other neuropeptides of the animal; (B) the (para)neoplastic change or cellular inflammatory response of the animal which involves obtaining data related to the value of cell cytotoxicity markers, cytokine and chemokine levels, immunoglobulin levels, type and amount of lymphocyte subsets and lymphocyte markers, and/or markers of (para)neoplastic change of the animal; (C) inherited organ dysfunction or dysplasia which involves obtaining data related to the value of the methyl malonic acid, the fucose-containing metabolites, blood or urine urate or uric acid

metabolites, normoglycemic glycosuria, amino acid uria, mannosidase containing cell metabolites, amyloid deposition in tissues, neuronal ceroid lipofuscin deposition, and deposition of gangliosides and/or other lysomal storage substrates of the animal; (D) autoimmune thyroiditis which involves obtaining data related to the value of a comprehensive thyroid autoantibody test **profile** , deoxyribonucleic acid fingerprint (gene map) for immunoglobulin receptors on B-cells, T-cell receptors, and protein products of the major histocompatibility complex genes (Class I and II allellic HLA, DLA or equivalent antigenic specificities) of the animal; (E) susceptibility to mammary cancer of the animal which involves obtaining data related to the value of estrogen (estradiol-17beta), estrogen receptors, interleukin (IL) 6, progesterone, and/or progesterone receptors of the animal; (F) integrity of immune surveillance mechanisms of the animal which involves obtaining data related to the value of the soluble and cellular inflammatory response mediators selectively at least one of the cytokine levels, chemokine levels, immonoglobulin levels, or lymphycyte subset markers; and (G) inherited bleeding disease or disorder of the animal which involves obtaining data related to the value of platelet count; platelet size; platelet morphology; prothrombin **time** ; partial thromboplastin **time** ; fibrinogen; fibrinfibrinogen degradation products; platelet **function tests** ; von Willebrand factor antigen and multimer analysis; specific coagulation factor analyses; fibrinolytic test; anti-thrombin III test; circulating anticoagulant tests, platelet factors 3 and 4; protein C; protein S; kinin-kinogen tests; prekallikein test; alpha1-antitrypsin assay; alpha2-macroglobulin assay; C1 esterase inactivator assay; anti-platelet antibody; and/or anti-megakaryocyte antibody tests.

INSTRUMENTATION AND TESTING - Preferred Device: The communication link includes the Internet. Data relating to the genotype data relating to the breed of the animal and background of the animal is also received in the database. The database is periodically updated with the laboratory test data and/or genetic data. A credit card information is provided to the remote user prior to provide the report after charging a credit card for such data. The communication also includes transferring money electronically via telecommunications line between respective financial entities related to the remote user and to an operator of the central database. The report is provided from the central base to the user after the transfer of money|

DE- <TITLE TERMS> HEALTH; **PROFILE** ; ANIMAL; HORSE; COMBINATION; GENETIC; DATA; ANIMAL; HEALTH; ASSESS; DATA; PERMIT; ANALYSE; PREDICT; HEALTH; DISEASE; DISORDER; PROBABILITY; LONGEVITY; ANIMAL|
DC- B04; C07; P31; S05; T01|
IC- <MAIN> A61B-005/00|
MC- <CPI> B04-B04D; B04-B04L; B04-H01; B04-P01; B11-C08E; B11-C09; B12-K04A ; C04-B04D; C04-B04L; C04-H01; C04-P01; C11-C08E; C11-C09; C12-K04A|
MC- <EPI> S05-D06; T01-J06A; T01-S03|
FS- CPI; EPI; EngPI||

14/4/23 (Item 23 from file: 350)
DIALOG(R)File 350:Derwent WPIX

AA- 2001-335566/200135|
XR- <XRAM> C01-103634|
TI- **Evaluating** a **biological condition** of a subject, involves deriving first **profile** data set from patient sample for quantitative measure of RNA or protein in a panel and producing calibrated **profile** data set for panel|
PA- SOURCE PRECISION MEDICINE INC (SOUR-N); TRYON V (TRYO-I)|
AU- <INVENTORS> BANKAITIS-DAVIS D M; BEVILACQUA M P; CHERONIS J; TRYON V|

NC- 094|
NP- 003|
PN- WO 200125473 A1 20010412 WO 2000US17846 A 20000628 200135 B|
PN- AU 200058985 A 20010510 AU 200058985 A 20000628 200143
PN- EP 1198585 A1 20020424 EP 2000944977 A 20000628 200235
<AN> WO 2000US17846 A 20000628|
AN- <LOCAL> WO 2000US17846 A 20000628; AU 200058985 A 20000628; EP 2000944977 A 20000628; WO 2000US17846 A 20000628|
AN- <PR> US 2000195522 P 20000407; US 99141542 P 19990628|
FD- WO 200125473 A1 C12Q-001/00
<DS> (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
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FD- AU 200058985 A C12Q-001/00 Based on patent WO 200125473
FD- EP 1198585 A1 C12Q-001/00 Based on patent WO 200125473
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LA- WO 200125473(E<PG> 117); EP 1198585(E)|
DS- <NATIONAL> AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW|
DS- <REGIONAL> AL; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LT; LU; LV; MC; MK; NL; PT; RO; SE; SI; EA; GH; GM; KE; LS; MW; MZ; OA; SD; SL; SZ; TZ; UG; ZW|
AB- <PN> WO 200125473 A1|
AB- <NV> NOVELTY - **Evaluating** (E) a **biological condition** of a subject, involves deriving, from the sample of RNAs and proteins, a first **profile** data set (I) and producing a calibrated **profile** data set (II) for the panel.|
AB- <BASIC> DETAILED DESCRIPTION - **Evaluating** (E) a **biological condition** of a subject, involves deriving, from the sample of RNAs and proteins, a first **profile** data set (I) having many members, each being a quantitative measure of distinct RNA or protein constituents in a panel of constituents selected, so that **measurement** of constituents enables **measurement** of the **condition** , and producing a calibrated **profile** data set (II) for the panel. Each member of (II) is a function of a corresponding member of (I) and a corresponding member of a baseline **profile** data set for the panel, the calibrated **profile** data set providing a **measure** of the **biological condition** of the subject.

INDEPENDENT CLAIMS are also included for the following:

(1) **evaluating** (E1) the effect on a **biological condition** by a first agent in relation to the effect by a second agent;

(2) conducting a clinical trial of an agent;

(3) a digital storage medium (III) on which is stored a computer readable calibrated **profile** data set, where the calibrated set relates to a sample having RNAs and/or proteins derived from a target cell population to which an agent has been administered, and calibrated **profile** data set includes a first number of members, each member being a quantitative measure of a change in an amount of a distinct RNA or protein constituent in a panel of constituents selected so that measurement of the constituents enables **measurement** of a **biological condition** as affected by administration of the agent;

(4) a digital storage medium (IIIa) on which is stored a number of records Ri relating to a population of subjects, each record Ri corresponding to a distinct instance Pi of a computer readable **profile** data set P, where each instance Pi of the **profile** data set P relates to a distinct sample derived from a subject, the sample having RNAs

and/or proteins, the **profile** data P set includes a number of members Mj, each record Ri includes, for each member Mij of a corresponding distinct instance Pi of the **profile** data set P, a value corresponding to the value of the member Mij, and each record Ri also includes a reference to a characteristic of the subject such as the age group, gender, ethnicity, geographic location, diet, medical disorder, clinical indicator, medication, physical activity, body mass or environmental exposure, relative to the record;

(5) **evaluating** (E2) a **biological condition** of a subject, based on a sample from the subject, the sample having RNAs and/or proteins, involves (E), accessing a data in a condition database having a number of records relating to a population of subjects, each record corresponding to a distinct instance of (II), and evaluating the first instance of (II) in relation to data in the condition database;

(6) displaying (D) a quantitative gene expression **analysis** data associated with **measurement** of a **biological condition** , by identifying (I) pertinent to the gene expression analysis data, producing (II) for the panel, and displaying (II) in a graphical format;

(7) a descriptive record (IV) of a change in a biological condition in a population of cells by a first set of numerical gene expression values for a panel of gene loci8) selecting a therapeutic agent from a class of therapeutic agents for administering to a subject so as to change a biological condition in a subject from a first biological condition to a second biological condition;

(9) characterizing the biological effectiveness of a single batch of a composition produced by a manufacturing process, by providing (II), and labeling the batch of the composition by placing (II) on each container in the batch optionally including the signature calibrated **profile** data set, and comparing (II) with a standardized calibrated **profile** data set;

(10) accessing biological information on (IIIa), by making the information available to a user;

(11) consumer evaluation of a product, which is dependent on a signature **profile** , by forming (IV), identifying the product using (IV), where the panel of gene loci is a signature panel and comparing (II) with an **average** calibrated **profile** data set to provide an explanation of the product;

(12) a computer program product for **evaluating** a **biological condition** of a subject or for **evaluating** a **biological condition** resulting from the use of an agent, including a computer usable medium having computer readable program code, where the computer program code comprises a program code for classifying a sample from the subject or the agent for an identifiable record, a program code for deriving (I), the **profile** data set being stored in the record, and a program code for optionally producing (II) for storage in the record;

(13) a computer system for **evaluating** a **biological condition** of a subject or for **evaluating** a **biological condition** resulting from the use of an agent, comprising a classification module for classifying a sample from the subject or the agent in an identifiable record, a derivative module for deriving (I), and a production module for producing (II); and

(14) **analyzing** a patient for a **biological condition** at a remote site, by providing a kit for measuring a **profile** data base for **evaluating** a **biological condition** .

USE - (E) is useful for diagnosing a biological condition of a subject, and for diagnosing a susceptibility for a biological condition. (E) is also useful for monitoring the progress of a biological condition and for establishing a descriptive record for an agent. The method further involves providing a mechanism of action for the composition, or metabolism for the composition. The composition further comprises a first compound and a second compound or a number of

compounds, and the biological activity results from any of synergism, interference or neutral interaction between the first and second compound. The biological activity of the compound is a toxic effect on the subject (claimed).

pp; 117 DwgNo 0/25|

AB- <TF> TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: **Evaluating** (E1) the effect on a **biological condition** by a first agent in relation to the effect by a second agent, by obtaining from first and second target population of cells to which the first and second agents have been respectively administered, first and second samples respectively, each sample having RNAs and/or proteins, deriving a first **profile** data set from the first sample and a second **profile** data set from the second sample, each set including a number of members, and producing for the panel a first calibrated **profile** data set and a second **profile** data set, where each member of the first calibrated **profile** data set is a function of a corresponding member of (I) and a corresponding member of a first baseline **profile** data set for the panel, and each of the second calibrated **profile** data set is a function of a corresponding member of the second **profile** data set and a corresponding member of a second baseline **profile** data set for the panel, the calibrated **profile** data sets providing a measure of the effect by the first agent on the biological condition in relation to the effect by the second agent. (E) optionally involves obtaining from the subject, a first sample having at least one of fluids, cells and active agents, applying the first sample or a portion to a defined population of indicator cells, obtaining from the indicator cells a second sample containing at least one of RNAs or proteins, or obtaining from a target population of cell to which the agent has been administered, a sample having RNAs and/or proteins. The sample is derived from blood and the baseline **profile** data set is derived from tissue or body fluid of the subject other than blood. The sample may also be derived from body fluid and tissue, blood, one of biopsy sample, needle aspirate, a lavage specimen, scraping or a surgical specimen, from tissue or fluid of a type distinct from that with respect to which the condition is clinically manifested. (E) further involves interpreting (II) in the context of at least one other clinical indicator selected from blood chemistry, urinalysis, X-ray, other chemical assays and physical findings. The biological condition is a complex disease process, involving multiple genes, the disease being of a type involving at least one of inflammation, auto-immune disease, degenerative disease, allergy, vascular disease, ischemia, cancer, developmental disease, hormonal condition, aging and infectious diseases, arthritis, asthma, multiple sclerosis, perimenopausal change and aging. The subject is a living organism, preferably a mammal. The biological condition concerns an organ or a system of the subject such as respiratory, vascular, nervous, metabolic, urinary, reproductive, structural, and immunological systems, and the panel of constituents enables **measurement** of the **condition** of the subject in relation to the organ or system. The panel includes at least half, preferably 80% conditions of the constituents of the Inflammation panel, Cell Growth and Differentiation Panel or Toxicity Panel. The number of constituents in the panel is at least three but less than 100. The agent is a drug, a mixture of compounds, functional food, a nutraceutical, therapeutic agent, allergen or a toxin. Each sample is derived from a target cell population to which has been administered an agent, such target cell population being derived from a subject. Accessing the condition database includes accessing the condition database over a global computer network. The method further involves supplementing the condition database based on data associated with the first instance of the (II). The first biological condition is a consequence of the adverse effects of any of an infectious agent, a biological warfare agent or an environmental agent and the second biological condition is

a reversal of these adverse effects. Deriving (I) from the sample includes hybridizing the sample with a set of nucleic acid probes that are attached to an insoluble matrix and the sample is applied to the matrix. (E) further involves evaluating the interaction of the agent with a second agent administered to the population of cells. The interaction is neutral, interference, cumulative or synergistic. The agent is a pharmaceutical agent, preferably a drug and the second agent is a complex mixture or a nutraceutical. Obtaining the sample and quantifying (I) are performed at a first location, and producing (II) includes using a network to access a database stored on a digital storage medium in a second location. The method further involves updating the database to reflect (I) quantified from the sample using a network which includes accessing a global computer network. The pool of subjects is selected using quantitative gene expression analysis on a number of candidates to identify those candidates likely to show a response to the agent. Administration includes determining dosage or dosage range by using a quantitative gene expression analysis. The method further involves using quantitative gene expression analysis to assist in **determining** at least one of **efficacy** and toxicity of the agent. Accessing biological information on (IIIa) further involves making the information available to the user on any of a network.

Preferred Function: The function of a member of (II) is other than a simple difference, second function of the ratio of the corresponding member of (I) to the corresponding member of the baseline **profile** data set, or logarithmic function. Each member of (II) is reproducible within one order of magnitude, preferably within 20% with respect to similar samples taken from the subject under similar conditions. Each member of (II) has biological significance, if it has a value differing by more than an amount D, where D=F(1.1)-F(.9), and F is the second function. The digital storage medium further comprises a large number of computer readable **profile** data sets, where each **profile** data set relates to a sample derived from a target cell population to which an agent has been administered, and the panel is the same for all **profile** data sets. The baseline **profile** data set is derived from one or more other samples from the same subject taken under conditions such as **time** , site or physiological condition, different from those of the sample. One or more other samples are taken over an interval of at least 12 months, preferably at least 1 month, between an initial sample and the sample. Each member of (II) is a function of a corresponding member of a post-administration data set and a corresponding member of a baseline data set. The function is a second function of the ratio of the member of baseline data set to the corresponding member of the post-administration data set. The library of descriptive records comprises a medical history for a single or a number of subjects or conditions. The library of signature **profile** data sets consist of signature **profile** data sets for a number of subjects.|

AB- <XA> EXAMPLE - No relevant example given.|

DE- <TITLE TERMS> EVALUATE; BIOLOGICAL; CONDITION; SUBJECT; DERIVATIVE; FIRST; **PROFILE** ; DATA; SET; PATIENT; SAMPLE; QUANTITATIVE; MEASURE; RNA; PROTEIN; PANEL; PRODUCE; CALIBRATE; **PROFILE** ; DATA; SET; PANEL|

DC- B04; D16|

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IC- <ADDITIONAL> C12Q-001/68|

MC- <CPI> B04-B04D4; B04-E03; B04-E05; B04-F02; B04-N04; B04-P01; B11-C08E; B11-C08E5; B12-K04A; B12-K04F; B12-M05; D05-H09; D05-H10|

FS- CPI||

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